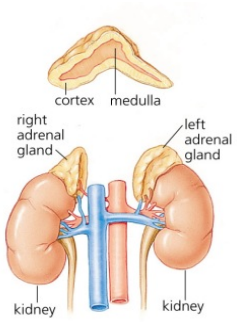
UNDERSTANDING CONGENITAL ADRENAL HYPERPLASIA

What is Congenital Adrenal Hyperplasia?

Congenital Adrenal Hyperplasia (CAH) is an imbalance in the hormones produced by the adrenal glands. The adrenal gland sits above the kidney – one on each side of the body. It is made up of the medulla (middle) and the adrenal cortex (outer), see photo. The medulla works normally in CAH making adrenaline. The adrenal cortex makes three main hormones called steroids. These steroids are necessary for normal health. It is the adrenal cortex and its steroids, which are involved in CAH.



What are the Three Steroids Involved in CAH?

The three steroids involved in CAH are cortisol, aldosterone and androgens.

Cortisol controls how the body copes with emotional stress or physical stress, such as infection or injury. Cortisol also helps maintain the blood sugar in the normal range and keep the blood pressure normal.

Aldosterone helps to regulate the salt levels in the body. Aldosterone causes the kidneys to keep salt if there is too little salt in the diet or if a lot of salt is lost due to excessive sweating. On the other hand, if a lot of salt is eaten, the adrenal cortex reduces the amount of aldosterone released, allowing the excess salt to be passed in the urine.

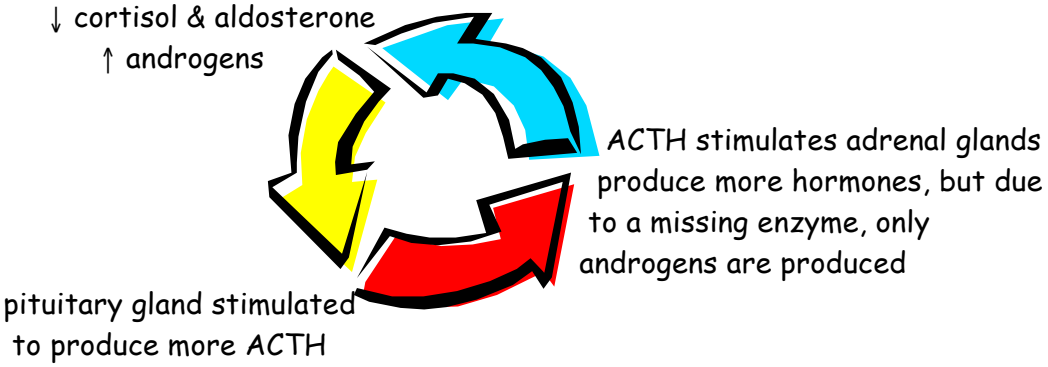
Androgens are a group of male hormones, one of which is testosterone. Androgens affect how the sexual organs develop before birth, and later, how the body matures at puberty.

The adrenal glands use cholesterol as their base material (main ingredient) for the hormones. By combining cholesterol with a series of different enzymes, the glands are able to transform cholesterol into aldosterone, cortisol and androgen. If enzymes are absent or in short supply, androgens will continue to be made even if there is block preventing them from being fully produced.

The health of the body depends on many things including a fine balance of the amounts of various hormones. The control center for maintaining the balance is a small gland in the center of the brain called the pituitary gland. This gland is the regulator that turns the adrenal glands on and off to control the hormone supply in the body. The pituitary gland turns the supply on by releasing the hormone ACTH (Adreno Cortico Tropic Hormone). When there is not enough cortisol or

aldosterone, the pituitary gland releases ACTH. This prompts the adrenal glands to transform cholesterol into more of the adrenal hormones.

However, in CAH cholesterol cannot be converted into cortisol and aldosterone and the adrenal glands are forced to make androgens. These high levels of androgens and low levels of cortisol and aldosterone signal the pituitary gland to release even more ACTH, which leads to an even further imbalance. This imbalance results in a lack of cortisol, a lack of aldosterone and excessive androgens.



Are There Different Types of CAH?

There are many types of CAH. The most common (80-90% of all cases) is **salt-losing CAH**. The loss of salt in the urine is uncontrolled (due to the low levels of aldosterone) and can cause dehydration, low blood pressure and vomiting. The levels of salt (sodium and chloride) and sugar (glucose) fall in the blood and potassium level rises. This can lead to an 'Adrenal Crisis' needing very urgent treatment as a potentially life threatening condition.

The less common type is **non-salt losing CAH**. In people with this type, the salt balance is normal. In stressful situations, however, some people with non-salt CAH may become salt losers and need extra treatment.

Another type of CAH is **late- onset CAH** or nonclassical. This type of CAH is a milder form of salt-losing CAH. People with late-onset CAH make enough cortisol and aldosterone, but they make excess androgens. Symptoms come and go, beginning at any time but typically in childhood or early adulthood. One common symptom of this type of CAH is excessive growth of body hair or erratic menstrual periods in women.

All of the types of CAH above are deficiencies of **enzyme 21-hydroxylase**. The next most common deficiency is of the **enzyme 11-beta hydroxylase**. Treatment

of this type of CAH is more complicated because high blood pressure can be severe if treatment is inadequate.

How does CAH affect the body?

Too little cortisol may cause tiredness and nausea. During illness or injury, low cortisol levels can lead to low blood pressure and even death.

The lack of aldosterone upsets salt levels. This imbalance may cause dehydration (too little fluid within the body), and possible death. Chronic salt imbalance may also cause abnormal growth.

Too much androgen causes abnormal physical development in children. Boys and girls with CAH may grow too fast; develop early pubic hair and acne, and stop growing too soon, causing short stature. Girls exposed to high levels of androgens before birth may have abnormal external genitalia at birth. Although their internal female organs are normal, excess androgens may also affect puberty and cause irregular menstrual periods.

While cortisol is essential for life, too much cortisol replacement also causes problems. Side effects of excessive cortisol replacement include obesity and short stature. Also, too much of the medicines (like hydrocortisone and Prednisone) that replace cortisol can lower bone density (osteoporosis), which can lead to fractures or changes in the bone such as avascular necrosis of the hip and raise cholesterol, blood pressure or blood sugar.

How is CAH Treated?

People with CAH have a normal life expectancy. For most people there is very little interference in every day life (if the condition is well managed). CAH is treated by replacing the hormones that the body is not able to make for itself. The aim of the treatment is to closely match the hormone levels that normal adrenal glands would make.

Cortisol is replaced by one of the family of medications called **glucocorticoids**. The generic names of the glucocorticoids are: Hydrocortisone, Injectable Hydrocortisone, Prednisolone, Prednisone, Methylprednisolone, and Dexamethasone.

The purpose of cortisol treatment in CAH is to replace the insufficient production of cortisol by the adrenal glands. Cortisol supplementation allows the body to recognize normal levels of cortisol in the body, which signals the adrenal glands to stop producing excessive amounts of androgens. Blood tests are done every six months to determine if the cortisol treatment is too low and consequently the androgens are too high. 17-hydroxyprogesterone, androstenedione and testosterone are the blood levels that

are monitored. More frequent blood tests may be needed during times of dose adjustment.

All people with salt losing CAH need to replace the lack of aldosterone. **Fludrocortisone** is given as the replacement. Too little fludrocortisone can cause low blood pressure and dizziness. Too much can cause high blood pressure and headaches. The correct level of fludrocortisone is determined by measuring blood pressure, potassium and the salt sensitive hormone renin.

What is an Adrenal Crisis?

An adrenal crisis occurs when the body needs a large amount of cortisol to deal with a major physical stress (such as severe flu or gastroenteritis) and none is available. The blood pressure and blood sugar will start to drop and the body can go into a state of shock. Signs of this are weakness and vomiting, drowsiness and loss of consciousness. An adrenal crisis is a life threatening medical emergency, which must be treated immediately.

This event is very rare and will probably never happen to most people with CAH who take treatment regularly, make appropriate increases in dose when ill, and seek help early if unexpectedly unwell or vomiting. If an adrenal crisis does occur, an injection of hydrocortisone should be given immediately. Admission to the hospital may also be necessary. If you are ever in doubt, always give an injection of hydrocortisone and then go to the nearest emergency room.

The dose of injectable hydrocortisone is large, but does not cause any side effects. The body uses it up in 6-8 hours. Keep in mind that the injection prevents the adrenal crisis but does nothing to treat the illness itself. You will need to seek treatment for the illness causing the adrenal crisis.

How do People get CAH?

CAH is an inborn error of metabolism. It is genetic. This means that the person has the disorder from the time they are conceived. At conception, the baby receives two sets of genetic material, one from the mother, and one from the father. This genetic material, called DNA, acts as a recipe for the baby's development. DNA includes information about the baby's eye and hair colour, sex and even whether the baby will be right or left-handed. DNA comes in units called genes. Each pair of genes gives directions to a certain part of the body.

In CAH, there is a problem with the genes that give information on how the body uses cholesterol. The disorder is caused by getting two copies of the faulty gene that gives the wrong instructions. One copy comes from the mother and one comes from the father. If the child inherits only one copy of the gene, they are a carrier for CAH but are not affected. There is a 1 in 4, or 25% chance that two carriers of the gene will have a baby with CAH. Boys and girls are equally affected.

Children born to carriers have:

- a 25% chance of having CAH
- a 50% chance of being a carrier and
- a 25% chance of being unaffected

With each pregnancy, there is the same 25% chance of having a child with CAH. In some families, there may be only one child with CAH, while in other families, multiple children may be affected.

Can Adults with CAH Pass the Disorder on to their Children?

Because CAH requires a carrier or recessive gene from each parent, the only way a person with CAH can have an affected child is to have children with a carrier or another person with the disorder.

Pregnancy

If a woman with CAH gets pregnant and is carrying a female fetus, high levels of androgens in the mom may possibly affect the baby. If you are a woman with CAH and think you might want to have children now or in the future, talk to the clinic staff about this for more information.

Helpful Resources

- The Adult Metabolic Diseases Clinic
  Vancouver General Hospital
  4th Floor, 2775 Laurel Street
  Vancouver, BC
  V5Z 1M9
  604-875-5965

- Magic Foundation
  www.magicfoundation.org

- CAH Family Support Network
  www.congenitaladrenalhyperplasia.org

- Congenital Adrenal Hyperplasia Research Education and Support www.caresfoundation.org

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